



References on Arthritis Research Using ALZET® Osmotic Pumps

- Q9406:** S. Park, *et al.* Intermittent fasting with a high-protein diet mitigated osteoarthritis symptoms by increasing lean body mass and reducing inflammation in osteoarthritic rats with Alzheimer's disease-like dementia. *British Journal of Nutrition* 2021;1-13
Agents: Amyloid protein, beta (25-35) **Vehicle:** Saline, sterile; **Route:** CSF/CNS (hippocampus); **Species:** Rat; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Dose (3 to 6 nmol/d); animal info (Sprague-Dawley female rats, 10 weeks, 235 g); Brain coordinates (lateral, -3.3 mm from the bregma; posterior, 2.0 mm from the midline; ventral, -2.5 mm from the dura); neurodegenerative (Alzheimer's disease);
- Q9384:** G. Nalesso, *et al.* Calcium calmodulin kinase II activity is required for cartilage homeostasis in osteoarthritis. *Scientific Reports* 2021;11(1):5682
Agents: KN-93 **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: Dose (5 umol/kg/day); Controls received mp w/ vehicle; animal info (Ten week old, male C57BL/6 mice); dependence;
- Q9507:** P. B. Tran, *et al.* Prolonged chemogenetic inhibition of nociceptors in a murine surgical model of osteoarthritis: effects on immune responses in dorsal root ganglia. *Osteoarthritis and Cartilage* 2020;28(**Agents:** Clozapine-N-oxide **Vehicle:** Saline; **Route:** Abdomen; **Species:** Mice; **Pump:** Not Stated; **Duration:** 6 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (10-week old male Nav1.8-Pdi C57BL/6 mice); Clozapine-N-oxide aka CNO; immunology;
- Q8551:** A. Jarneborn, *et al.* Tofacitinib treatment aggravates Staphylococcus aureus septic arthritis, but attenuates sepsis and enterotoxin induced shock in mice. *Scientific Reports* 2020;10(1):10891
Agents: Tofacitinib **Vehicle:** DMSO; PEG 300; Water; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 3 days;
ALZET Comments: Dose (15 mg/kg/day); 10% Peg 300, 40% water used; Controls received mp w/ vehicle; animal info (Female NMRI mice and female BALB/c mice, 6-12 weeks old); dependence;
- Q7656:** H. J. Qin, *et al.* SDF-1/CXCR4 axis coordinates crosstalk between subchondral bone and articular cartilage in osteoarthritis pathogenesis. *Bone and Mineral* 2019;125(140-150
Agents: AMD3100 **Vehicle:** Saline; **Route:** Bone (tibia); **Species:** Mice; Rat; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: Dose (180 µg/day); Controls received mp w/ vehicle; animal info ((Mice 3 months, male, C57BL/6J), (Rat 3 months, male, Sprague-Dawley)); pumps were implanted directly in subchondral bone;
- Q7272:** F. Bai, *et al.* Spinal Cord Glycine Transporter 2 Mediates Bilateral ST35 Acupoints Sensitization in Rats with Knee Osteoarthritis. *Evidence-Based Complementary and Alternative Medicine* 2019;2019(7493286
Agents: Glycine **Vehicle:** Saline; **Route:** CSF/CNS (Intrathecal); **Species:** Rat; **Pump:** 2002; **Duration:** 14 Days;
ALZET Comments: Dose (0.1 umol/h); Controls received mp w/ vehicle; animal info (Male Sprague-Dawley rats, 200-250 g); behavioral testing (PWMT test);
- Q8129:** M. Miyoshi, *et al.* Efficacy of constant long-term delivery of YM-58483 for the treatment of rheumatoid arthritis. *Eur J Pharmacol* 2018;824(89-98
Agents: Antagonist of Ca²⁺ release-activated Ca²⁺ (CRAC) channels **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** Not stated; **Duration:** 28 days;
ALZET Comments: Dose (0.5 ug/kg/day); Controls received mp w/ vehicle; animal info (Male, 6-10 weeks old, 30 g); Antagonist of Ca⁺ release-activated Ca²⁺ channels aka YM-58483; dependence;
- Q6522:** S. C. van Dalen, *et al.* Interleukin-1 is not involved in synovial inflammation and cartilage destruction in collagenase-induced osteoarthritis. *Osteoarthritis Cartilage* 2017;25(3):385-396
Agents: Interleukin-1 receptor antagonist **Vehicle:** Saline; **Route:** IP; **Species:** Mice; **Pump:** 1007D; **Duration:** 2 weeks;
ALZET Comments: Dose (37.5 ug/hr); Controls received empty mp; animal info (12 week old female C57BL/6 mice);



- Q5917:** D. J. Wilkinson, *et al.* Matriptase Induction of Metalloproteinase-Dependent Aggrecanolytic In Vitro and In Vivo: Promotion of Osteoarthritic Cartilage Damage by Multiple Mechanisms. *Arthritis Research & Therapy* 2017;69(8):1601-1611
Agents: Antibody A11; compound 59 **Vehicle:** Saline; **Route:** IP, SC; **Species:** Mice; **Pump:** 1004, 2004; **Duration:** 4 weeks, 8 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6J, 25-30g); pumps replaced every 4 weeks; Dose (Antibody: 1.5 ug/day; Compound 59: 5, 25, or 50 mg/kg/day);
- Q6532:** K. Wang, *et al.* T140 blocks the SDF-1/CXCR4 signaling pathway and prevents cartilage degeneration in an osteoarthritis disease model. *PLoS One* 2017;12(4):e0176048
Agents: T140 **Vehicle:** PBS; **Route:** SC; **Species:** Guinea pig; **Pump:** 2006; **Duration:** Not Stated;
ALZET Comments: Dose (180 ug/d); Controls received mp w/ vehicle; animal info (9 month old male Hartley guinea pigs weighing about 600g); pumps replaced every 6 weeks; Therapeutic indication (osteoarthritis);
- Q5974:** H. Shimaoka, *et al.* A cytokine signal inhibitor for rheumatoid arthritis enhances cancer metastasis via depletion of NK cells in an experimental lung metastasis mouse model of colon cancer. *Oncol Lett* 2017;14(3):3019-3027
Agents: Tofacitinib **Vehicle:** PEG 300; **Route:** CSF/CNS; **Species:** Mice; **Pump:** 2002; **Duration:** 6 days;
ALZET Comments: animal info (Wild-type CD1) ; Controls received mp w/vehicle; dose (15 mg/kg/day); cancer; enzyme inhibitor (JAK3)
- Q6216:** S. Liu, *et al.* Efficiency and Safety of CRAC Inhibitors in Human Rheumatoid Arthritis Xenograft Models. *J Immunol* 2017;199(5):1584-1595
Agents: Antibody (hCRACM1-IgG); YM-58483 **Vehicle:** Saline; Intralipose; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 28 days;
ALZET Comments: hCRACM1-IgG Dose (1 or 10 mg/kg), YM058483 Dose (1.5mg/kg); YM-58483 was mixed with 10% Intralipose, which is an i.v. lipid emulsion containing 10% soybean oil, 1.2% egg yolk phospholipids, and 2.2% glycerin; Controls received mp w/ vehicle; hCRACM1-IgG is a neutralizing monoclonal antibody targeting human CRACM1; YM-58483 is a small molecular CRAC blocker; Immunology (transplant);
- Q6439:** J. Lee, *et al.* Nicotine drives neutrophil extracellular traps formation and accelerates collagen-induced arthritis. *Rheumatology (Oxford)* 2017;56(4):644-653
Agents: Nicotine **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 2006; **Duration:** 42 days;
ALZET Comments: Dose (15 mg/kg/day); Controls received mp w/ vehicle; animal info (male DBA/1J mice);
- Q6440:** M. G. Ledesma-Colunga, *et al.* Prolactin blocks the expression of receptor activator of nuclear factor kappaB ligand and reduces osteoclastogenesis and bone loss in murine inflammatory arthritis. *ASAIO Journal* 2017;19(1):93
Agents: Prolactin **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 28 days;
ALZET Comments: animal info (Male Sprague-Dawley rats weighing 200–250 g);
- Q6304:** A. Kaneguchi, *et al.* Nociception contributes to the formation of myogenic contracture in the early phase of adjuvant-induced arthritis in a rat knee. *J Orthop Res* 2017;35(7):1404-1413
Agents: Morphine hydrochloride **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 5 days;
ALZET Comments: Dose (41–48 mg/kg/day); animal info (8-week-old male Wistar rats weighing 200–240 g); Therapeutic indication (Knee arthritis);
- Q6456:** M. Ito, *et al.* A novel JAK inhibitor, peficitinib, demonstrates potent efficacy in a rat adjuvant-induced arthritis model. *J Pharmacol Sci* 2017;133(1):25-33
Agents: Peficitinib **Vehicle:** PEG, Acetic acid; **Route:** IP; **Species:** Rat; **Pump:** 2ML2; **Duration:** Not Stated;
ALZET Comments: Dose (0.12, 0.24, and 0.48 mg/day per body); Controls received mp w/ vehicle; Resultant plasma level (7.0 ng/mL, 18 ng/mL, and 35 ng/mL on day 13, and 7.1 ng/mL, 13 ng/mL, and 30 ng/mL on day 16);



Q6010: Y. Chen, *et al.* Attenuation of subchondral bone abnormal changes in osteoarthritis by inhibition of SDF-1 signaling. *Osteoarthritis Cartilage* 2017;25(6):986-994

Agents: AMD3100 **Vehicle:** PBS; **Route:** SC; **Species:** Rat; **Pump:** 2006; **Duration:** 6 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (16 weeks old, Sprague-Dawley; 400-500 g); Therapeutic indication (Osteoarthritis, subchondral bone); Dose (22.3 mg/ml);

Q6608: W. Lu, *et al.* CXCL12/CXCR4 Axis Regulates Aggrecanase Activation and Cartilage Degradation in a Post-Traumatic Osteoarthritis Rat Model. *Int J Mol Sci* 2016;17(10):

Agents: AMD3100 **Vehicle:** PBS; **Route:** Not Stated; **Species:** Rat; **Pump:** 2004; **Duration:** 8 weeks;

ALZET Comments: Dose (3 mg/day); Controls received mp w/ vehicle; animal info (8 week old male Sprague-Dawley rats weighing 190-210g); pumps replaced every 4 weeks; Therapeutic indication (osteoarthritis);

Q4897: Gisela Segond von Banchet, *et al.* Long-Lasting Activation of the Transcription Factor CREB in Sensory Neurons by Interleukin-1b During Antigen-Induced Arthritis in Rats. *Arthritis & Rheumatology* 2016;68(2):532-541

Agents: Anakinra **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 26 days;

ALZET Comments: Controls received mp w/ saline; animal info (female, Lewis, 6-8 weeks old, 160-180g); animal info (female, Lewis, 6-8 weeks old, 160-180g); immunology; delayed delivery for 5 days; Dose (53 mg/kg/day);

Q5339: Y. Dong, *et al.* Inhibition of SDF-1alpha/CXCR4 Signalling in Subchondral Bone Attenuates Post-Traumatic Osteoarthritis. *Int J Mol Sci* 2016;17(6):

Agents: AMD3100 **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 30 days;

ALZET Comments: Controls received mp w/ vehicle and sham operation; animal info (C57BL/6J mice (30 males, 2 months old)); immunology; (AMD3100 is an immunostimulant); inhibitor of CXCR4; transected the anterior cruciate ligament on the right knee; caused joint instability; Dose (180 ug/day);

Q8183: Y. Chen, *et al.* Translational potential of ginsenoside Rb1 in managing progression of osteoarthritis. *J Orthop Translat* 2016;6(27-33)

Agents: Retinoblastoma **Vehicle:** Ethanol; **Route:** SC; **Species:** Rat; **Pump:** 2006; **Duration:** 4 weeks;

ALZET Comments: animal info (16-week-old male Sprague-Dawley rats, weighing 450-500 g); Retinoblastoma aka Rb1; dependence;

Q4613: N. P. Thomas, *et al.* Attenuation of cartilage pathogenesis in post-traumatic osteoarthritis (PTOA) in mice by blocking the stromal derived factor 1 receptor (CXCR4) with the specific inhibitor, AMD3100. *JOURNAL OF ORTHOPAEDIC RESEARCH* 2015;33(1071-1078)

Agents: AMD3100 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 2 months;

ALZET Comments: Controls received mp w/ PBS or empty pumps; animal info (male, C57BL6J, 2 months old); pumps replaced every 4 weeks;

Q4279: M. Radwan, *et al.* Protection against murine osteoarthritis by inhibition of the 26S proteasome and lysine-48 linked ubiquitination. *Annals of the Rheumatic Diseases* 2015;74(1580-1587)

Agents: MG132 **Vehicle:** DMSO; PEG 300; **Route:** SC; **Species:** Mice; **Pump:** 1004; **Duration:** 8 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (C57BL6J or mutant-Ub transgenic, 8 weeks old); pumps replaced every 4 weeks; 50% DMSO used; 50% PEG 300; enzyme inhibitor (proteasome, general);

Q4547: F. R. Nieto, *et al.* Calcitonin Gene-Related Peptide-Expressing Sensory Neurons and Spinal Microglial Reactivity Contribute to Pain States in Collagen-Induced Arthritis. *Arthritis & Rheumatology* 2015;67(1668-1677)

Agents: Calcitonin gene-related peptide (8-37) **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (female, Lewis, 180-200g); behavioral testing (Von Frey filaments; Plantar test); immunology; peptides;



- Q3829:** G. Kato, *et al.* The inhibitory effects of a RANKL-binding peptide on articular and periarticular bone loss in a murine model of collagen-induced arthritis: a bone histomorphometric study. *Arthritis Research & Therapy* 2015;17(U2-U15)
Agents: Peptide, OP3-4 **Vehicle:** PBS; DMSO; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 49 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, DBA/1J, 7 weeks old); pumps replaced after day 35 or 42; 20% DMSO used; peptides; "a sustained-release carrier for OP3-4 needs to be developed since peptide drugs are unstable and aggregate easily in vivo. The effects of OP3-4 in this study were achieved using infusion pumps" pg 13
- Q4440:** C. B. Hamilton, *et al.* Weight-bearing asymmetry and vertical activity differences in a rat model of post-traumatic knee osteoarthritis. *OSTEOARTHRITIS AND CARTILAGE* 2015;23(1178-1185)
Agents: Water, distilled **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 8 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, Sprague Dawley, 301-325g); pumps replaced every 4 weeks; post op. care (buprenorphine 50 ug/kg SC); behavioral testing (static weight bearing, exploratory motor behavior); long-term study;
- Q5121:** C. T. Appleton, *et al.* Reduction in disease progression by inhibition of transforming growth factor alpha-CCL2 signaling in experimental posttraumatic osteoarthritis. *Arthritis & Rheumatology* 2015;67(10):2691-701
Agents: AG1478; RS504393 **Vehicle:** DMSO; water, deionized; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 10 weeks;
ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by plasma levels and knee articular cartilage; pumps replaced every 4 weeks; %50 of DMSO; long-term study; enzyme inhibitor (EGFR and CCR2 inhibitors); EGFR inhibitor AG1478, CCR2 inhibitor RS504393; Dose: (AG1478) 21 nmoles/kg/hour; (RS504393) 200 nmoles/kg/hour
- Q4022:** K. Nishimura, *et al.* Tofacitinib Facilitates the Expansion of Myeloid-Derived Suppressor Cells and Ameliorates Arthritis in SKG Mice. *Arthritis & Rheumatology* 2014;66(S1271-S1272)
Agents: Tofacitinib **Vehicle:** DMSO; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 5 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (female, SKG mice, arthritis induction); immunology; enzyme inhibitor (JAK3)
- Q3980:** G. J. Litherland, *et al.* Glycogen Synthase Kinase 3 Inhibition Stimulates Human Cartilage Destruction and Exacerbates Murine Osteoarthritis. *Arthritis & Rheumatology* 2014;66(2175-2187)
Agents: CT99021 **Vehicle:** DMSO; PEG 400; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6J, 10 weeks old); 50% PEG 400 used; 50% DMSO used; CT99021 is a GSK-3 inhibitor;
- Q3906:** B. D. Furman, *et al.* Targeting pro-inflammatory cytokines following joint injury: acute intra-articular inhibition of interleukin-1 following knee injury prevents post-traumatic arthritis. *Arthritis Research & Therapy* 2014;16(U305-U319)
Agents: Interleukin-1 receptor antagonist **Vehicle:** Saline; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 4 weeks;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, C57BL6, 8 weeks old); functionality of mp verified by serum levels; comparison of injection vs mp; stress/adverse reaction: (see pg. 4); post op. care (buprenorphine); "...no significant differences were detected for any of the outcome measures in mice receiving systemic saline via osmotic pump or IP injections.." pg 4; pumps removed after 28 days;
- Q3460:** M. E. Dowty, *et al.* Preclinical to Clinical Translation of Tofacitinib, a Janus Kinase Inhibitor, in Rheumatoid Arthritis. *Journal of Pharmacology and Experimental Therapeutics* 2014;348(1):165-173
Agents: Tofacitinib **Vehicle:** DMSO; PEG 300; **Route:** SC; **Species:** Mice; **Pump:** Not Stated; **Duration:** 36 days;
ALZET Comments: Controls received mp w/ vehicle; animal info (male, DBA/1, 10-12 weeks old); functionality of mp verified by plasma levels; pumps replaced every 19 days; 33% DMSO used; dose-response (pg. 168); toxicology; immunology; Tofacitinib is a janus kinase inhibitor; enzyme inhibitor (JAK3)
- Q3045:** N. Adan, *et al.* Prolactin promotes cartilage survival and attenuates inflammation in inflammatory arthritis. *Journal of Clinical Investigation* 2013;123(9):3902-3913
Agents: Prolactin, ovine **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 6 days; 21 days;
ALZET Comments: Animal info (male, Sprague Dawley, 200-250g); functionality of mp verified by serum levels at 21 days; behavioral testing (hind paw pain); immunology;



Q2910: F. Y. Wei, *et al.* Attenuation of osteoarthritis via blockade of the SDF-1/CXCR4 signaling pathway. *Arthritis Research & Therapy* 2012;14(4):U233-U243

Agents: AMD 3100 **Vehicle:** PBS; **Route:** SC; **Species:** Guinea pig; **Pump:** 2006; **Duration:** 12 weeks;

ALZET Comments: Controls received mp w/ PBS; animal info (0.88 kg +/- 0.21 kg); pumps replaced once every 6 weeks; long-term study

Q2585: E. Schurgers, *et al.* Pulmonary inflammation in mice with collagen-induced arthritis is conditioned by complete Freund's adjuvant and regulated by endogenous IFN- γ . *European Journal of Immunology* 2012;42(12):3223-3234

Agents: Etanercept **Vehicle:** PBS; **Route:** Not Stated; **Species:** Mice; **Pump:** 2004; **Duration:** Not Stated;

ALZET Comments: Control animals received mp w/ vehicle; animal info (IFN gamma R KO, DBA/1)

Q2259: A. K. Clark, *et al.* Spinal cathepsin S and fractalkine contribute to chronic pain in the collagen-induced arthritis model. *Arthritis & Rheumatology* 2012;64(6):2038-2047

Agents: Cathepsin S; fractalkine **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2001; **Duration:** Not Stated;

ALZET Comments: Animal info (adult, female, Lewis, 180-200 g); peptides

Q1778: D. Y. Liu, *et al.* Population pharmacokinetic-pharmacodynamic-disease progression model for effects of anakinra in Lewis rats with collagen-induced arthritis. *JOURNAL OF PHARMACOKINETICS AND PHARMACODYNAMICS* 2011;38(6):769-786

Agents: Anakinra **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 1 week;

ALZET Comments: Animal info (male, Lewis, 6-9 wks old); half-life "4-6 hours" pg 78; pharmacokinetic study; pk study

Q1059: L. Evans, *et al.* Suppression of Leukocyte Infiltration and Cartilage Degradation by Selective Inhibition of Pre B-Cell Colony-Enhancing Factor/Visfatin/Nicotinamide Phosphoribosyltransferase APO866-Mediated Therapy in Human Fibroblasts and Murine Collagen-Induced Arthritis. *Arthritis & Rheumatology* 2011;63(7):1866-1877

Agents: APO866 **Vehicle:** Propylene glycol; saline; **Route:** SC; **Species:** Mice; **Pump:** 1002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; animal info (male, DBA/1, 7-8 wks old); half-life (~8 hours in humans pg 1876); APO866 is a small molecule inhibitor in human fibroblasts in vitro and in murine collagen arthritis; A maximum tolerated dose of APO866 of 0.126 mg/m²/hour in human clinical trials and 0.18 mg/m²/hour in rats has been reported" pg 1868

Q0010: P. Ergang, *et al.* Local metabolism of glucocorticoids and its role in rat adjuvant arthritis. *Molecular and Cellular Endocrinology* 2010;323(2):155-160

Agents: Anakinra **Vehicle:** Saline; Sodium citrate; EDTA; Tween 80; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Controls received vehicle; animal info (male, Lewis, 7-9 weeks old; adjuvant-induced arthritis); IL-1B antagonist; 0.5mM EDTA; 0.1% Tween 80

P9904: M. K. Boettger, *et al.* Spinal Tumor Necrosis Factor alpha-Neutralization Reduces Peripheral Inflammation and Hyperalgesia and Suppresses Autonomic Responses in Experimental Arthritis A Role for Spinal Tumor Necrosis Factor alpha-During Induction and Maintenance of Peripheral Inflammation. *Arthritis & Rheumatology* 2010;62(5):1308-1318

Agents: Etanercept **Vehicle:** Not Stated; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2ML4; **Duration:** 3, 21 days;

ALZET Comments: Controls received mp w/vehicle: animal info (Lewis, 6-8 wks, 160-180 g); ALZET intrathecal catheter used; schematic drawing with ALZET pump and catheter

Q0005: M. K. Boettger, *et al.* Spinally applied ketamine or morphine attenuate peripheral inflammation and hyperalgesia in acute and chronic phases of experimental arthritis. *Brain, Behavior; Immunity* 2010;24(3):474-485

Agents: Ketamine; Morphine **Vehicle:** Saline; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2ML4; **Duration:** 21 days;

ALZET Comments: Controls received mp w/ vehicle; tolerance; ALZET brain infusion kit used; half-life pg 477 (2.5 hrs in CSF (ketamine); 2.1 hrs (morphine)); animal info (Female, Lewis, 6-8 wks old, 160-180 g); dorsal laminectomy; behavioral testing (pain related behavior)



P9905: M. Stolina, *et al.* RANKL inhibition by osteoprotegerin prevents bone loss without affecting local or systemic inflammation parameters in two rat arthritis models: comparison with anti-TNF-alpha or anti-IL-1 therapies. *Arthritis Research & Therapy* 2009;11(6):U251-U265

Agents: Anakinra **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Animal info (Lewis, 7 to 8 wks old, AIA, CJA)

P9023: A. J. Milici, *et al.* Cartilage preservation by inhibition of Janus kinase 3 in two rodent models of rheumatoid arthritis. *Arthritis Research & Therapy* 2008;10(1):U175-U183

Agents: CP-690550 **Vehicle:** PEG 300; **Route:** SC; **Species:** Rat; Mice; **Pump:** 2004; 2ML2; **Duration:** 2 weeks; 28 days;

ALZET Comments: Controls received mp w/ vehicle or no pump; dose-response (fig. 1); enzyme inhibitor (JAK3, janus kinase 3); animal info (male, DBA/J1, male, Lewis); "it was necessary to administer CP-690550 via osmotic pumps due to the poor (PK) properties of this compound in rodents."

P8953: A. Knedla, *et al.* The therapeutic use of osmotic minipumps in the severe combined immunodeficiency (SCID) mouse model for rheumatoid arthritis. *Annals of the Rheumatic Diseases* 2008;68(1):124-129

Agents: Interleukin-10; interleukin-1 receptor antagonist **Vehicle:** Saline; DMSO; **Route:** SC; **Species:** Mice (SCID); **Pump:** 2004; **Duration:** 40 days;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by plasma levels; good methods (p.125); peptides; animal info (female, SCID, 4-5 wks old); Rheumatoid arthritis; pump and technique schematics p. 125; stability (with an excellent description of methods) was verified for 40 days @ 37C; 50% DMSO used; "... the application of proteins via osmotic pumps is an affective tool to evaluate the effects of cytokines and inhibitors in vitro." p. 128

P9761: E. Dahlen, *et al.* Development of interleukin-1 receptor antagonist mutants with enhanced antagonistic activity in vitro and improved therapeutic efficacy in collagen-induced arthritis. *Journal of Immunotoxicology* 2008;5(2):189-199

Agents: Anakinra **Vehicle:** NaCl; citric acid; EDTA; tween 80; **Route:** IP; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: Anakinra is an interleukin-1 receptor antagonist; 0.35mM EDTA; 0.07% Tween 80;

P9287: E. Brahn, *et al.* An Angiogenesis Inhibitor, 2-Methoxyestradiol, Involutes Rat Collagen-Induced Arthritis and Suppresses Gene Expression of Synovial Vascular Endothelial Growth Factor and Basic Fibroblast Growth Factor. *Journal of Rheumatology* 2008;35(11):2119-2128

Agents: Estradiol, 2-methoxy- **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** 18 days;

ALZET Comments: Controls received mp w/ vehicle; comparison of oral gavage vs. mp; animal info (syngeneic LOU, 8-10 wks old, 100-150 g., Collagen-induced arthritis; "Delivery of 60 mg/kg by an osmotic pump, however, was similar in efficacy to 300 mg/kg oral gavage. This result suggests that a steady-state level of 2ME2 achieved equivalent arthritic inhibition at a lower total dose." (p. 2124)

P8929: N. Badlani, *et al.* The protective effect of OP-1 on articular cartilage in the development of osteoarthritis. *Osteoarthritis and Cartilage* 2008;16(5):600-606

Agents: Osteogenic protein-1 **Vehicle:** Lactose; **Route:** Knee (articular cavity); **Species:** Rabbit; **Pump:** 2004; **Duration:** 6 weeks;

ALZET Comments: Controls received mp w/ vehicle; functionality of mp verified by separate in vivo test; peptides; post op. care ("appropriate"); animal info (New Zealand, White, 1 yr old); also known as BMP-7 or bone morphogenic protein-7; catheter was secured with polyethylene stents; "The efficacy of the (ALZET Pump) was tested in vivo before beginning the study with good results"; "constant infusion of OP-1 may be the most ideal form of delivery"; long-term study; good methods

P9324: S. Averill, *et al.* Reg-2 expression in dorsal root ganglion neurons after adjuvant-induced monoarthritis. *Neuroscience* 2008;155(4):1227-1236

Agents: Nerve growth factor, recomb. human; glial-derived neurotrophic factor, recomb. human; leukemia inhibitory factor, recomb. human **Vehicle:** Saline; Albumin, rat serum; **Route:** CSF/CNS (intrathecal); **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; peptides, animal info (male, Wistar, 220-400 g.)



R0248: H. Tsutsumi, *et al.* Inhibitors of the chemokine receptor CXCR4: Chemotherapy of AIDS, metastatic cancer, leukemia and rheumatoid arthritis. *Letters in Drug Design & Discovery* 2007;4(1):20-26

Agents: TN14003, 4F-benzoyl- **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; Mice (SCID); **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: Cancer (breast carcinoma); immunology; peptides; CXCR4 antagonist; review, see p. 21, 23

P8525: H. Saito, *et al.* A tumor necrosis factor receptor loop peptide mimic inhibits bone destruction to the same extent as anti-tumor necrosis factor monoclonal antibody in murine collagen-induced arthritis. *Arthritis & Rheumatology* 2007;56(4):1164-1174

Agents: Peptide, WP9QY; antibody, monoclonal, anti-TNF alpha **Vehicle:** PBS; DMSO; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 19 days;

ALZET Comments: Controls received mp w/ vehicle; dose-response (fig. 1); pumps replaced every 7 days; half-life (p. 1182) "short;" peptides; animal info (male, DBA/1J, 6 weeks old, collagen induced arthritis); 10% DMSO

P8965: H. Matsuno, *et al.* Requirement of methotrexate in combination with anti-tumor necrosis factor alpha therapy for adequate suppression of osteoclastogenesis in rheumatoid arthritis. *Journal of Rheumatology* 2007;34(12):2326-2333

Agents: Infliximab; immunoglobulin G, human **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (SCID); **Pump:** Not Stated; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ human IgG; immunology; animal info (SCID-HuRAG-pit, 6-7 wks old; TNF-alpha inhibitor

P8793: D. Kurosaka, *et al.* The effect of endostatin evaluated in an experimental animal model of collagen-induced arthritis. *Scandinavian Journal of Rheumatology* 2007;36(6):434-441

Agents: Endostatin **Vehicle:** PBS; **Route:** IP; **Species:** Mice; **Pump:** Not Stated; **Duration:** 2 weeks;

ALZET Comments: Controls received mp w/ vehicle; animal info (1J, 6 week); "compared with the once daily dosing regimen, the administration of endostatin by an osmotic pump achieved a similar arthritis-inhibiting effect at one-tenth of the dose...the administration method using osmotic pump is useful." pg. 434

P8454: L. Geboes, *et al.* Freund's complete adjuvant induces arthritis in mice lacking a functional interferon-gamma receptor by triggering tumor necrosis factor alpha-driven osteoclastogenesis. *Arthritis & Rheumatology* 2007;56(8):2595-2607

Agents: Etanercept **Vehicle:** Water, sterile; **Route:** SC; **Species:** Mice; **Pump:** 2004; **Duration:** 28 days;

ALZET Comments: Controls received mp w/vehicle; animal info (male, DBA/1, wt, IFN γ R-KO, 8-12 weeks old)

P7770: C. M. Paulos, *et al.* Folate-targeted immunotherapy effectively treats established adjuvant and collagen-induced arthritis. *Arthritis Research & Therapy* 2006;8(3):U243-U252

Agents: Anakinra **Vehicle:** Not Stated; **Route:** SC; **Species:** Rat; **Pump:** Not Stated; **Duration:** 4 weeks;

ALZET Comments: Animal info (female, Lewis, 200g.)

P7678: G. Q. Guan, *et al.* Estrogenic effect on swelling and monocytic receptor expression in an arthritic temporomandibular joint model. *Journal of Steroid Biochemistry and Molecular Biology* 2005;97(3):241-250

Agents: Estradiol, 17B- **Vehicle:** PEG; **Route:** Not Stated; **Species:** Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Animal info (OVX, Sprague-Dawley, 200-225 g, female)

P7446: G. Gaitan, *et al.* Enhancement of fentanyl antinociception by subeffective doses of nitroparacetamol (NCX-701) in acute nociception and in carrageenan-induced monoarthritis. *Life Sciences* 2005;77(1):85-95

Agents: Fentanyl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 5 days;

ALZET Comments: Controls received mp w/ vehicle; tolerance; animal info (male, Wistar, 250-320 g)

P7498: B. De Klerck, *et al.* Pro-inflammatory properties of stromal cell-derived factor-1 (CXCL12) in collagen-induced arthritis. *Arthritis & Rheumatology* 2005;7(6):R1208-R1220

Agents: AMD 3100 **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ PBS; immunology; animal info (male, 8-12 weeks)



P6677: J. Zwerina, *et al.* Single and combined inhibition of tumor necrosis factor, interleukin-1, and RANKL pathways in tumor necrosis factor-induced arthritis - Effects on synovial inflammation, bone erosion, and cartilage destruction. *Arthritis & Rheumatology* 2004;50(1):277-290

Agents: Interleukin-1 receptor antagonist **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice (transgenic); **Pump:** 2004; **Duration:** 4 weeks;

ALZET Comments:

P6767: H. Tamamura, *et al.* Identification of a CXCR4 antagonist, a T140 analog, as an anti-rheumatoid arthritis agent. *FEBS Letters* 2004;569(1-3):99-104

Agents: TN14003, 4F-benzoyl- **Vehicle:** PBS; **Route:** SC; **Species:** Mice; **Pump:** 1007D; 2002; **Duration:** 7,14 days;

ALZET Comments: Controls received mp w/ vehicle; dose-response (Fig.2); immunology; peptides

P7427: S. U. Simjee, *et al.* Modulation of the gait deficit in arthritic rats by infusions of muscimol and bicuculline. *Pain* 2004;109(453-460)

Agents: Muscimol; Bicuculline **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;

ALZET Comments: Controls received mp w/ vehicle; dose-response; no stress (see pg. 455-6)

R0219: W. B. Van Den Berg. Is there a rationale for combined TNF and IL-1 blocking in arthritis? *Clinical and Experimental Rheumatology* 2002;20(Suppl. 28):S21-S25

Agents: Insulin-like growth factor I, receptor antagonist **Vehicle:** Not Stated; **Route:** Not Stated; **Species:** Mice; **Pump:** Not Stated; **Duration:** Not Stated;

ALZET Comments: "In mice full protection is only achieved with continued dosing in ALZET minipumps." (p. S-24)

P5046: A. Scharstuhl, *et al.* Inhibition of endogenous TGF-beta during experimental osteoarthritis prevents osteophyte formation and impairs cartilage repair. *Journal of Immunology* 2002;169(507-514)

Agents: Transforming Growth Factor-B2, soluble receptor **Vehicle:** Polymyxin B; **Route:** IP; **Species:** Mice; **Pump:** 1007D; 2002; **Duration:** 7,14 ,21 days;

ALZET Comments: Arthritis; controls received empty pumps or mp w/ vehicle; functionality of mp verified by residual aspiration; pumps replaced after 14 days; stability verified by ELISA after infusion (p. 508, 510); soluble TGF-B RII selectively inhibits transforming growth factor-B; peptides; polymyxin B included as endotoxin inhibitor; 2002 pumps used for 7 and 14 day administration, 21-day group received a 1007D pump for final 7 days

P5094: H. Matsuno, *et al.* The role of TNF-alpha in the pathogenesis of inflammation and joint destruction in rheumatoid arthritis (RA): a study using a human RA/SCID mouse chimera. *Rheumatology* 2002;41(329-337)

Agents: Tumor necrosis factor-a; Interleukin-6 **Vehicle:** Serum, fetal bovine; Culture medium, RPMI 1640; **Route:** SC; **Species:** Mice (SCID); **Pump:** 1007D; **Duration:** 7 days;

ALZET Comments: controls received mp w/ vehicle; functionality of mp verified by serum cytokine levels; immunology; peptides; cytokines were recombinant; pump incorrectly called an osmium pump (p. 331); agents administered singly.

P5978: A. Luttun, *et al.* Revascularization of ischemic tissues by PIGF treatment, and inhibition of tumor angiogenesis, arthritis and atherosclerosis by anti-Flt1. *Nature Medicine* 2002;8(8):831-840

Agents: Placental growth factor; vascular endothelial growth factor **Vehicle:** Not Stated; **Route:** SC; **Species:** Mice; **Pump:** 2001; **Duration:** 7 days;

ALZET Comments: Angiogenesis

P5458: A. Coxon, *et al.* Inhibition of interleukin-1 but not tumor necrosis factor suppresses neovascularization in rat models of corneal angiogenesis and adjuvant arthritis. *Arthritis & Rheumatology* 2002;46(10):2604-2612

Agents: Interleukin-1 receptor antagonist **Vehicle:** Saline; sodium citrate; EDTA; Tween 80; **Route:** SC; **Species:** Rat; **Pump:** 2ML1; **Duration:** 7 days;

ALZET Comments: Controls received mp w/ BSA "to control for nonspecific anti-angiogenic effects of stress associated with implantation of the osmotic minipump." (p. 2605); implantation of pumps delivering BSA caused no angiogenesis; 0.5mM EDTA; 0.1% Tween 80;



R0169: S. B. Abramson, *et al.* Blocking the effects of IL-1 in rheumatoid arthritis protects bone and cartilage. *Rheumatology* 2002;41(9):972-980

Agents: Not Stated **Vehicle:** Not Stated; **Route:** SC; **Species:** Rabbit; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Peptides

Q6819: J. Braz, *et al.* Therapeutic Efficacy in Experimental Polyarthritis of Viral-Driven Enkephalin Overproduction in Sensory Neurons. *The Journal of Neuroscience* 2001;21(20):7881-7888

Agents: Naloxone; Naloxone methiodide **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2001; **Duration:** 3 days;
ALZET Comments: Dose (3 mg/kg/day); Controls received mp w/ vehicle; animal info (polyarthritic male sprawg dawley rats, 6 weeks old); behavioral testing (foot withdrawal (pain)); Therapeutic indication (Rheumatoid arthritis);

P4412: R. E. Voll, *et al.* Amelioration of type II collagen induced arthritis in rats by treatment with sodium diethyldithiocarbamate. *The Journal of Rheumatology* 1999;26(6):1352-1358

Agents: Diethyldithiocarbamate, Sodium **Vehicle:** PBS, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2002; 2ML2; **Duration:** 7, 9 days;
ALZET Comments: Controls received mp w/vehicle; functionality of mp verified by plasma levels; comparison of IP injections vs. mp; agent also called Ditiocarb or DDTC; arthritis

P4417: J. Dawson, *et al.* Effects of soluble interleukin-1 type II receptor on rabbit antigen-induced arthritis: clinical, biochemical and histological assessment. *Rheumatology* 1999;38(401-406)

Agents: Interleukin-1 receptor **Vehicle:** Saline; **Route:** SC; **Species:** Rabbit; **Pump:** Not Stated; **Duration:** 14 days;
ALZET Comments: Controls received mp w/vehicle; functionality of mp verified by plasma levels; immunology; peptides; arthritis; soluble interleukin-1 type II receptor used

P3724: C. J. Blais, *et al.* Involvement of endogenous kinins in the pathogenesis of peptidoglycan-induced arthritis in the lewis rat. *Arthritis & Rheumatology* 1997;40(7):1327-1333

Agents: Hoe 140; Bradykinin, Lys-Leu8-des-Arg9 **Vehicle:** Saline, sterile; **Route:** SC; **Species:** Rat; **Pump:** 1007D; **Duration:** 6 days;
ALZET Comments: controls received mp w/ vehicle; peptides; agents administered singly and in combination

P3568: S. Persson, *et al.* Interleukin-10 suppresses the development of collagen type II-induced arthritis and ameliorates sustained arthritis in rats. *Scand. J. Immunol* 1996;44(607-614)

Agents: Interleukin-10 **Vehicle:** PBS, sterile; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 14 days;
ALZET Comments: controls received mp w/ PBS; comparison of footpad injections vs. mp; immunology; peptides

P6296: L. A. B. Joosten, *et al.* Anticytokine Treatment Of Established Type II Collagen-Induced Arthritis in DBA/1 Mice. *Arthritis & Rheumatology* 1996;39(5):797-809

Agents: Interleukin-1 receptor antagonist, recomb. human **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** 1007D; **Duration:** 7 days;
ALZET Comments: Controls received mp w/ BSA; immunology

P3563: P. L. E. M. Van Lent, *et al.* Major role for interleukin 1 but not for tumor necrosis factor in early cartilage damage in immune complex arthritis in mice. *J. Rheumatol* 1995;22(2250-2258)

Agents: Interleukin-1 receptor antagonist **Vehicle:** Not Stated; **Route:** IP; **Species:** Mice; **Pump:** 1007D; **Duration:** Not Stated;
ALZET Comments: Controls received empty pumps or mp w/ vehicle; immunology

P4079: A. A. J. van de Loo, *et al.* Role of interleukin-1 in antigen-induced exacerbations of murine arthritis. *American Journal of Pathology* 1995;146(1):239-249

Agents: Interleukin-1 receptor antagonist **Vehicle:** Not Stated; **Route:** IP; **Species:** Not Stated; **Pump:** Not Stated; **Duration:** 7 days;
ALZET Comments: brief mention of mp on p. 247; immunology



P3995: S. J. Oliver, *et al.* Suppression of collagen-induced arthritis by an angiogenesis inhibitor, AGM-1470, in combination with cyclosporin: reduction of vascular endothelial growth factor (VEGF). *Cellular Immunology* 1995;166(196-206

Agents: Cyclosporin A **Vehicle:** PEG 300; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;

ALZET Comments: Photo of rat showing implanted pump (pg. 204); no stress (see pp. 199, 204, 205); immunology; controls received sham surgeries

P3379: J. G. Conway, *et al.* Inhibition of cartilage and bone destruction in adjuvant arthritis in the rat by a matrix metalloproteinase inhibitor. *J. Exp. Med* 1995;182(449-457

Agents: GI168 **Vehicle:** DMSO; Sodium citrate buffer; **Route:** SC; **Species:** Rat; **Pump:** 2ML2; **Duration:** 2 weeks;

ALZET Comments: controls received mp w/vehicle; dose-response (see p. 451); immunology; multiple pumps per animal (2); "GI168 had poor oral bioavailability and a short plasma t 1/2 after subcutaneous injection... so minipump delivery was evaluated." p. 451; enzyme inhibitor (matrix metalloproteinase)

P2940: J. R. Earl, *et al.* Proinflammatory effects of morphine in the rat adjuvant arthritis model. *Int. J. Tiss. Reac* 1994;XVI(4):163-170

Agents: Morphine sulfate; Naloxone HCl **Vehicle:** Saline; **Route:** SC; **Species:** Rat; **Pump:** 2ML4; **Duration:** Not Stated;

ALZET Comments: Controls received mp with saline or were naive

P3096: D. O. Willenborg, *et al.* Inhibition of adjuvant arthritis in the rat by phosphosugars and the α -glucosidase inhibitor castanospermine. *Immunol. Cell Biology* 1992;70(369-377

Agents: Castanospermine; Mannose, D-; Phosphate, mannose-6-; Phosphate, fructose-1- **Vehicle:** Saline; **Route:** SC; IP;

Species: Rat; **Pump:** 2002; **Duration:** 14 days;

ALZET Comments: controls received mp with saline or sham operation; comparison of drinking water admin. of CS vs. mp; immunology

P2361: F. J.-P. Miao, *et al.* Chronically administered nicotine attenuates bradykinin-induced plasma extravasation and aggravates arthritis-induced joint injury in the rat. *Neuroscience* 1992;51(3):649-655

Agents: Nicotine hydrogen tartrate; ICI-118,551 Hexamethonium chloride **Vehicle:** Saline; Ethanol; **Route:** SC; **Species:** Rat;

Pump: 2ML2; 2ML4; **Duration:** 16,30 days;

ALZET Comments: comparison of sc injections vs. mp; immunology; ICI-118,551 is a β_2 -adrenoceptor antagonist; antihypertensive

P2020: E. Brahn, *et al.* Effects of tumor necrosis factor alpha (TNF- α) on collagen arthritis. *Lymphokine Cytokine Res* 1992;11(5):253-256

Agents: Tumor necrosis factor- α **Vehicle:** Albumin, bovine serum; Water; **Route:** Not Stated; **Species:** Rat; **Pump:** 2ML4;

Duration: 28 days;

ALZET Comments: peptides

P1956: M. Mihara, *et al.* Interleukin 6 inhibits delayed-type hypersensitivity and the development of adjuvant arthritis. *European Journal of Immunology* 1991;21(2327-2331

Agents: Interleukin-6 **Vehicle:** PBS; Serum, mouse; **Route:** SC; **Species:** Mice; **Pump:** 2ML2; 2ML4; **Duration:** 2, 4 weeks;

ALZET Comments: Immunology; peptides

P1837: H. Lorberboum-Galski, *et al.* Administration of IL-2-PE40 via osmotic pumps prevents adjuvant induced arthritis in rats. Improved therapeutic index of IL-2-PE40 administered by continuous infusion. *Int. J. Immunopharmac* 1991;13(2/3):305-315

Agents: Interleukin-2, PE40 **Vehicle:** NAD; **Route:** IP; **Species:** Rat; **Pump:** 2001; **Duration:** Not Stated;

ALZET Comments: Functionality of mp verified by serum levels of IL-2-PE40; comparison of bid ip injections vs. mp; no stress (see pg. 314); stability achieved for 6 days by adding NAD (p. 308); multiple pumps per animal (2); half-life of 1-2 hours when given ip